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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/918,589	07/30/2001	Cale M. Halbleib	IVGN 437	2015
65482	7590	11/27/2006	EXAMINER	
INVITROGEN CORPORATION C/O INTELLEVATE P.O. BOX 52050 MINNEAPOLIS, MN 55402			SHAHER, SHULAMITH H	
			ART UNIT	PAPER NUMBER
			1647	

DATE MAILED: 11/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/918,589

Applicant(s)

HALBLEIB ET AL.

Examiner

Shulamith H. Shafer, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 18 September 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 18, 19, 22, 24, 30-32 and 35-37 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) 18, 19, 22, 24, 30-32, 35-37 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

### **Detailed Action**

#### ***Status of Application, Amendments, And/Or Claims:***

Applicant's response of 18 September 2006 to the Office Action of 6 June 2006 has been received and entered.

The amendment to the specification has been received and entered. Claims 33 and 34 have been cancelled. Claim 32 has been amended and the amendment has been entered. New claims 36 and 37 have been presented and entered. Claims 18, 19, 22, 24, 30-32, 35-37 are pending in the instant application.

The text of those sections of Title 35, U. S. Code not included in this action can be found in a prior Office action.

### **Withdrawn Objections/Rejections**

The objection to the title is withdrawn in view of applicants' amendment to the title.

The objection to the IDS is withdrawn in view of applicants' arguments.

The rejection of Claims 18, 19, 22, 24, 30-32 and 35 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of applicants' amendment to the claims.

### **Maintained/New Rejections**

#### ***35 U.S.C. §103***

The rejection of Claims 18, 24, 32 and 35 under 35 U.S.C. 103(a) as being unpatentable over Bolger et al. (1998, WO 98/05962) in view of Roeder et al. (2001, US Patent No. 6,248,520, filed 6 July 1998), Burbaum et al. (1999, US Patent No. 5,876,946), and Kirkemo et al. (1985, US Patent No. 4,510,251) is maintained for

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reasons of record in previous office actions of 6 February 2006 and 6 June 2006 and for reasons set forth below.

Applicants traverse this rejection (response of 18 September 2006, page 9, section A). The reason for the traversal is that Compound 4 disclosed by Kirkemo et al. in the '251 patent is not a pregen, but a pregnane, specifically 11,17,21-trihydroxypregane-3,20-dione; therefore the '251 patent does not disclose the steroid recited in the wherein clause of the independent claim, claim 32.

Applicant's arguments have been fully considered but are not found to be persuasive for the following reasons. The text of the '251 patent (column 8, lines 21-34) teaches the structure as a cortisol-aminomethyl fluorescein derivative. The starting material is disclosed as cortisol-3-carboxymethyloxime. Cortisol has a double bond in the 4-5 position (See enclosed copy of communication from CAS help desk, dated 15 November, 2006). Absent evidence to the contrary, the drawing of Compound 4 is in error in omitting double bond in the 4-5, position, and the text identifies the correct structure.

The rejection of Claim 19 under 35 U.S.C. 103(a) as being unpatentable over Bolger in view of Roeder, Burbaum and Kirkemo as applied to claim 32 and further in view of Chen (2000 US Patent No. 6,054,295) is maintained for reasons of record (Office Action of 6 June 2006) and for reasons set forth below.

Applicants traverse this rejection (response of 18 September 2006, page 10, section B). The reason for the traversal is that Compound 4 disclosed by Kirkemo et al. in the '251 patent is not a pregen, but a pregnane, specifically 11,17,21-trihydroxypregane-3,20-dione; therefore the '251 patent does not disclose the steroid recited in the wherein clause of the independent claim, claim 32; Chen ('295 patent) does not overcome this deficiency.

Applicant's arguments have been fully considered but are not found to be persuasive for the following reasons. As stated above, the text of the '251 patent (column 8, lines 21-34) teaches the structure as a cortisol-aminomethyl fluorescein derivative. The starting material is disclosed as cortisol-3-carboxymethyloxime.

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Cortisol has a double bond in the 4-5 position. Absent evidence to the contrary, the drawing of Compound 4 is in error in omitting double bond in the 4-5, position, and the text identifies the correct structure.

The rejection of Claims 22 and 30 under 35 U.S.C. 103(a) as being unpatentable over Bolger et al. in view of Roeder et al, Burbaum et al, and Kirkemo et al. as applied to claim 32 and further in view of Tanaka et al (1997, Glia 20:23-37) is maintained for reasons of record (Office Action of 6 June 2006) and for reasons set forth below.

Applicants traverse this rejection (response of 18 September 2006, page 10, section C). The reason for the traversal is that Compound 4 disclosed by Kirkemo et al. in the '251 patent is not a pregen, but a pregnane, specifically 11,17,21-trihydroxypregane-3,20-dione; therefore the '251 patent does not disclose the steroid recited in the wherein clause of the independent claim, claim 32; Tanaka et al. does not overcome this deficiency.

Applicant's arguments have been fully considered but are not found to be persuasive for the following reasons. As stated above, the text of the '251 patent (column 8, lines 21-34) teaches the structure as a cortisol-aminomethyl fluorescein derivative. The starting material is disclosed as cortisol-3-carboxymethyloxime. Cortisol has a double bond in the 4-5 position. Absent evidence to the contrary, the drawing of Compound 4 is in error in omitting double bond in the 4-5, position, and the text identifies the correct structure.

The rejection of Claim 31 under 35 U.S.C. 103(a) as being unpatentable over Bolger et al. Roeder et al, Burbaum et al and Kirkemo et al. as applied to claim 32 above and further in view of Bhakta et al (1992, Arch Biochem Biophys 292:303-310) is maintained for reasons of record (Office Action of 6 June 2006) and for reasons set forth below.

Applicants traverse this rejection (response of 18 September 2006, page 11, section D). The reason for the traversal is that Compound 4 disclosed by Kirkemo et al. in the '251 patent is not a pregen, but a pregnane, specifically 11,17,21-

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trihydroxypregane-3,20-dione; therefore the '251 patent does not disclose the steroid recited in the wherein clause of the independent claim, claim 32; Nath et al. does not overcome this deficiency.

Applicant's arguments have been fully considered but are not found to be persuasive for the following reasons. As stated above, the text of the '251 patent (column 8, lines 21-34) teaches the structure as a cortisol-aminomethyl fluorescein derivative. The starting material is disclosed as cortisol-3-carboxymethyloxime. Cortisol has a double bond in the 4-5 position. Absent evidence to the contrary, the drawing of Compound 4 is in error in omitting double bond in the 4-5, position, and the text identifies the correct structure.

Claims 18, 24, 32 and 35 and newly presented claims 36 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bolger et al., Roeder et al. and Burbaum et al. in view of Adamczyk et al. (1997. Tetrahedron 53:12855-12866).

The teachings of Bolger et al., Roeder et al. and Burbaum et al. are discussed in detail in previous office actions of 6 February 2006 and 6 June 2006.

However, the references cited above do not teach a method for monitoring a binding interaction of a steroid hormone receptor with a test ligand wherein the steroid hormone receptor ligand includes a steroid selected from the group consisting of a 5 $\alpha$ -androstan derivatized at one or more of the 1, 3, 6, 7, 11, 15, 17, 18, or 19 positions with a linker conjugated to a fluorescent label; a 4-androsten derivatized at one or more of the 1, 3, 6, 7, 11, 15, 17, 18, or 19 positions with a linker conjugated to a fluorescent label; 4-pregnen derivatized at one or more of the 3, 6, 7, 11, 17, 19, 20 or 21 positions with a linker conjugated to a fluorescent label; and a dexamethasone derivatized at position 21 with a linker conjugated to a fluorescent label (Claim 32) or wherein the steroid hormone receptor ligand includes a steroid selected from the group consisting of a 5 $\alpha$ -androstan derivatized at one or more of the 1, 3, 6, 7, 11, 15, 17, 18, or 19 positions with a linker conjugated to a fluorescent label; a 4-androsten derivatized at one or more of the 1, 3, 6, 7, 11, 15, 17, 18, or 19 positions with a linker conjugated to a fluorescent label; 4-pregnen derivatized at one or more of the 6, 7, 11, 17, 19, 20 or 21

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positions with a linker conjugated to a fluorescent label; and a dexamethasone derivatized at position 21 with a linker conjugated to a fluorescent label (claim 36) or wherein the steroid hormone receptor ligand includes a steroid selected from the group consisting of a 5 $\alpha$ -androstan derivatized at one or more of the 1, 3, 6, 7, 11, 15, 17, 18, or 19 positions with a linker conjugated to a fluorescent label; a 4-androsten derivatized at one or more of the 1, 3, 6, 7, 11, 15, 17, 18, or 19 positions with a linker conjugated to a fluorescent label; and a dexamethasone derivatized at position 21 with a linker conjugated to a fluorescent label (claim 37).

Adamczyk et al. teach preparation of fluorescent tracers for the development of an immunoassay for quantification of testosterone by fluorescence polarization immunoassay (abstract). Among the compounds taught is a 4-androsten derivatized at position 1 with a linker conjugated to a fluorescent label (page 12859, last compound, second figure and page 12862, last paragraph, bridging 12863, 1<sup>st</sup> paragraph).

It would have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to utilize the nuclear hormone receptors taught by Roeder et al, in the method of measuring competitive binding activity of molecules to steroid hormone receptors taught by Bolger et al, including the fluorescently-labelled 4-androsten derivative taught by Adamczyk et al. in the reaction mixture. The person of ordinary skill in the art would have been motivated to make these modifications because the Adamczyk et al. teach that these derivatives may be employed in fluorescence polarization assays. One would reasonably expect success because Bolger et al teach the success of this method utilizing steroid receptors.

### **Conclusions**

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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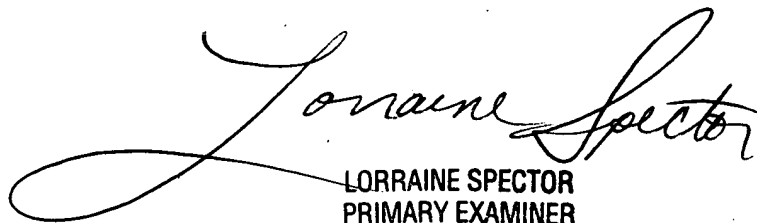
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shulamith H. Shafer, Ph.D. whose telephone number is 571-272-3332. The examiner can normally be reached on Monday through Friday, 8 AM to 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SHS

  
LORRAINE SPECTOR  
PRIMARY EXAMINER